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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/501,730 02/10/00 SHERMAN

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EXAMINER

PAK, Y

ART UNIT

PAPER NUMBER

1652

DATE MAILED:

04/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/501,730

Applicant(s)

SHERMAN ET AL.

Examiner

Yong Pak

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) 11-16 and 29-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 17-28 and 33 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claims ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____.

DETAILED ACTION

Claims 1-33 are pending.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-28 and 33, drawn to uricase, classified in class 435, subclass 190.
- II. Claims 29-32, drawn to method of purifying uricase, classified in class 530, subclass 413.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the method of Invention II can purify other proteins that form large aggregates. Furthermore, uricase can be isolated and purified by standard biochemical methods.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and recognized divergent subject matter, restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species of the claimed invention: mammalian, fungal or microbial, invertebrate, and

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plant uricase. These four uricases are different organisms, each with its own function, properties and utility.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-2, 11, 13, and 15 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Mr. Dale Hunt on January 8, 2001 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-28 and 33, with an election to mammalian uricase. Applicant in replying to this Office action must make affirmation of this election. Claims 29-32 and 11-16 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

Entry that is lined through on form PTO-1449 filed on January 19, 2001 fails to comply with the provisions of 37 CFR 1.98 (see MPEP § 609) because reference of Donadio et al. is in a foreign language and there is no concise explanation of the relevance as required by 37 CFR 1.98(3) for each document listed on from PTO-1449 that is not in the English language.

Drawings

Drawings filed concurrently with the application has been objected by the Draftsman. Please refer to the attached PTO-948 form for details.

Claim Objections

Claim 10 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 10 ultimately depends on claim 1, which encompasses only full-length enzymes and not fragments. However, claim 10 is drawn to a fragment that is not within the scope of claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 8, 9, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 5 and 9, it is unclear which specific amino acid sequences are encompassed by the claim. The metes and bounds of the claim are unclear because various polypeptides can be "substantially" the sequence of a porcine, bovine, ovine, or baboon liver uricase and many polypeptides can contain a portion of porcine and baboon liver uricases.

Claim 8 is unclear because the recitation of "PKS" is not an art accepted term. Amending claim 8 to recite a sequence with the mutations being made would obviate this rejection. For example, R291K/T301S mutant of SEQ ID NO:3. ✓

Regarding claim 9, without the recitation of the SEQ ID NO, it is unclear in which sequence Tyr is at position 97. ✓

Regarding claim 10, any amino acid sequence comprises of an amino and carboxyl terminus. Therefore, "...comprises an amino terminal and a carboxy terminus" appears to be redundant.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Wu et al.

Wu et al. (form PTO-1449) teach recombinant porcine urate oxidase from *S. scrofa* (page 9412). Wu et al. also teach recombinant *P. hamadryas* urate oxidase (page 9412-9413). The two uricases were purified to homogeneity with a subunit of 35 kDa for both porcine and baboon uricases and therefore the uricases are free of aggregates larger than octamers. Regarding claim 33, patentability of a product does

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not depend on the method used in producing the product (MPEP 2113). Therefore, the enzymes of Wu et al. anticipate claims 1-5 and 33.

Claims 1-2, 4 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Alvares et al.

Alvares et al. teach uricase from rat liver (page 4909, 5th paragraph and page 4912, 2nd paragraph). The uricase of Alvares et al. is 35kDa, which corresponds to one subunit, and active at pH11 (page 4912, 5th paragraph) and thus the enzyme is free of aggregates larger than octamers. Therefore, the uricase of Alvares et al. anticipates claims 1-5 and 33.

Claims 1, 4, 17-22, 25-17, and 33 are rejected under 35 U.S.C. 102(a) as being anticipated by Caliceti et al.

Caliceti et al. teach uricase from *Candida utilis* purified to homogeneity with a molecular weight of 130 kDa, (page 639, 2nd paragraph and page 640, Table 1). The uricase of Caliceti is free of aggregates larger than octamers because it is well known in the art that uricase from *C. utilis* exists as a tetramer with subunit of about 30 kDa. Regarding claims 4 and 33, patentability of a product does not depend on the method used in producing the product (MPEP 2113).

Regarding claims 17-19 and 25-26, Caliceti et al. teach uricase conjugated to linear monomethoxy poly(ethylene glycol) or mPEG and branched mPEG (page 639, 4th paragraph), wherein the conjugation is via an amine linkage (page 639, 4th and 5th

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paragraph). Regarding claims 20-22, Caliceti et al. teach uricase conjugated to a PEG wherein PEG has a molecular weight of 5 kDa and 10 kDa (page 640, 2nd paragraph) and 3 PEG per uricase subunit (page 640, Table 1). Regarding claim 27, Caliceti et al. teach a pharmaceutical composition comprising uricase in a carrier (page 639, 5th paragraph). Therefore, the teachings of Caliceti et al. anticipates claims 1, 4, 17-22, 25-27, and 33

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7, 9 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al.

Wu et al. teach porcine and baboon uricase, as discussed above. However, Wu et al. do not teach chimeric uricase and baboon uricase in which His has replaced Try 97.

Wu et al. teach that baboon, porcine and mouse uricases are highly conserved (page 9413, 2nd column and Fig 2 -b). Mouse and porcine uricase has a His at position 97, while baboon has a Tyr at position 97. A portion can be construed as one or more amino acids.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a chimeric uricase by replacing Tyr 97 of the baboon uricase with Try97 of the porcine uricase. One would be motivated to replace a residue with a conserved residue because conserved amino acids very often impart the characteristic property of an enzyme. One of ordinary skill in the art would have had a reasonable expectation of success since site specific mutations are routinely performed in the art.

Claims 1-5, 10 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al.

Wu et al. teach porcine and baboon uricase, as discussed above. However, Wu et al. do not teach uricase truncated at one or both termini.

However, Wu et al. teach that porcine urate oxidase is six amino acid residues shorter than that of rat uricase (page 9414, 2nd column) but the two uricases are highly conserved throughout the coding region (page 9413, 4th paragraph).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a functional uricase of a smaller size by deleting residues from both N -terminus. The motivation is to determine whether residues at the N-terminus are important for uricase activity and to use a smaller functional fragment of uricase in view of convenience.

Claims 1, 17-27, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caliceti et al.

Caliceti et al. teach uricase conjugated to PEG, as discussed above. Caliceti et al. do not teach 6-10 PEG per uricase subunit.

However, Caliceti et al. teach that activated PEG polymers have different reactivity and different protein/polymer ratios is needed.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a uricase conjugated to different number of PEG. The motivation is to overcome different reactivity of the activated polymers when conjugated to uricase.

Claims 1, 17-22, 27-28, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caliceti et al.

Caliceti et al. teach uricase conjugated to PEG, as discussed above. Caliceti et al. do not teach a pharmaceutical composition stabilized by lyophilization.

Compositions used as pharmaceuticals are generally lyophilized to prolong shelf life and to conveniently store in dosage amounts before solubilizing in suitable solution.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make uricase conjugated to PEG in dry form to solubilize in solutions suitable for intravenous or parenterally administrations. The motivation is to prolong the shelf life of PEG-uricase.

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4534.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Yong Pak
Patent Examiner

April 2, 2001


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